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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/617,099	07/14/2000	Susumu Seino	P19771	5279

7590 10/22/2002

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EXAMINER
MITRA, RITA

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/22/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/617,099	SEINO ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6 and 8-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Applicants' amendment and response to office action dated March 27, 2002, filed on June 27, 2002 (paper #12) is acknowledged. Claims 7, 11 and 12 have been cancelled. Claims 3-6 and 9 have been amended. Therefore, claims 3-6 and 8-10 are currently pending and are under examination.

Response to Remarks and Arguments

Withdrawal of Rejections

The rejection of claims 3, 5-7 under **35 U.S.C. § 101** is withdrawn in view of Applicants' amendment to claims 3, 5 and 6 and cancellation of claim 7.

The rejection of claims 7, 11 and 12 under **35 U.S.C. § 112, first paragraph** is moot in view of Applicants' cancellation of these claims.

The rejection of claim 9 under **35 U.S.C. § 112, first paragraph** is withdrawn in view of Applicants' amendment to the claim.

The rejection of claims 4-12 under **35 U.S.C. § 112, second paragraph** as being broaden the scope of claim 3 is withdrawn in view of Applicants' amendment to claims 3, 4, 5, 6 and 9. The rejection of claims 7, 11 and 12 is moot because of the cancellation of the claims.

The rejection of claims 3-5 under **35 U.S.C. § 112, second paragraph** as being dependent upon non-elected claims is withdrawn in view of Applicants' amendment to claims 3-5.

The rejection of claims 4 and 5 under **35 U.S.C. § 112, second paragraph** as being indefinite for the use of the term "under" is withdrawn in view of Applicants' amendment to claims 4 and 5.

The rejection of claims 6 and 7 under **35 U.S.C. § 112, second paragraph** as being lacking antecedent basis is withdrawn in view of Applicants' amendment to claim 6 and cancellation of claim 7.

The rejection of claims 4-12 under **35 U.S.C. § 102 and 103** as being anticipated by or in the alternative, as obvious over Wang et al. is withdrawn in view of Applicants' submitting a verified translation of the priority document, filed October 8, 1999 and thereby removing Wang et al. from the prior art.

Maintenance of Rejections

Rejections under 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 and 8-10 remain/are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a full length DNA set forth in SEQ ID NO: 2 encoding the protein of SEQ ID NO: 1; does not reasonably provide enablement for all mutants or fragments generated from any position located on the sequence of SEQ ID NO: 1 or SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants' reasons and arguments in response to the rejection are fully considered, however they are not found persuasive. The traversal is addressed along with the rejection as set forth below:

Claims 3-6, 8-10 encompass a mouse DNA that encodes a protein having the amino acid sequence set forth in SEQ ID NO: 1 (claim 3), a DNA having a nucleotide sequence set forth in SEQ ID NO: 2 (claims 4 and 6), a DNA having a nucleotide sequence with one to ten nucleotides deleted, substituted, inserted or added relative to the nucleotide sequence set forth in SEQ ID NO: 2 and encoding the protein having the amino acid sequence of SEQ ID NO: 1 (claims 5), a fragment of nucleotide sequence set forth in SEQ ID NO: 2 (claim 8), a probe comprising a DNA fragment comprising a part of the DNA of SEQ ID NO: 2 (claim 9), a primer DNA fragment consisting of a partial sequence of the sequence of SEQ ID NO: 2 (claim 10). The

specification, however, only discloses cursory conclusions (see page 4-5), without data to support the findings, which state that a mouse gene that encodes the protein of SEQ ID NO: 1. and a mutant thereof, which has a property of interacting with a GDP/GTP exchange factor II. There are no indicia that the present application enables the full scope in view of the DNA encoding the protein of SEQ ID NO: 1 and a mutant thereof as discussed in the following stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is encompassed.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breadth of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the state of the prior art; and, 8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) The nature of the invention:

The nature of the invention is defined by the claims, which include a mouse DNA encoding a protein set forth in SEQ ID NO: 1 and a mutant thereof. However the specification does not provide the information on the structure and function of the claimed mutants.

2) The breadth of the claims:

The breadth of the claims is broad and encompasses an unspecified amount of variants regarding the DNA's protein products of SEQ ID NO: 1 as biological active fragments, which are not specifically described or demonstrated in the specification.

Claim 3 is drawn to a mouse DNA that encodes the protein of SEQ ID NO: 1. Specification on pages 4-5 gives a description about a mouse gene that encodes a protein having an amino acid sequence set forth in SEQ ID NO: 1 and a mutant thereof, which has a property of interacting with a GDP/GTP exchange factor II. The specification does not provide a sequence of

a mouse DNA mutant that has a property of interacting with a GDP/GTP exchange factor II. For these reasons, it requires undue experimentation to make the claimed invention, especially where in claim 5, any one to ten nucleotides, singly or in any combination of insertion, deletion and substitution would have been included by the claim and for which the specification does not describe with particularity as to retention of function.

Claim 5, which is directed to a DNA having a nucleotide sequence with one to ten nucleotides deleted, substituted, inserted or added relative to the nucleic acid sequence set forth in SEQ ID NO: 2. Specification while defining "one or more" indicates at page 5 that several (e.g. 3 or 4) to 10 nucleotides relative to SEQ ID NO: 2 would be modified, and at page 7 specification provides a general description on how a variety of mutants can be generated. However, the specification fails to provide any specific description of the structure and function of the mutants generated. While the specification in Example (page 14, lines 15-22, Fig. 4), and at page 9, lines 4-16 describes and demonstrates that the full length DNA set forth in SEQ ID NO: 2 encoding the protein of SEQ ID NO: 1 has a property to interact with cAMP-GEFII, there is no disclosure about the biological activities of the claimed mutants.

Applicants response (page 5, last paragraph) states that one of ordinary skill in the art, having both the nucleotide sequence set forth in SEQ ID NO: 2 and the amino acid sequence set forth in SEQ ID NO: 1 could easily make 1-10 mutations to SEQ ID NO: 2 and create a DNA which encodes SEQ ID NO: 1 using a genetic code Table. The arguments are considered but not found persuasive because the claim reads 1-10 nucleotides deleted, substituted, inserted or added relative to the nucleotide sequence of SEQ ID NO: 2, that has the amino acid sequence of SEQ ID NO: 1. Therefore, it is not just 1-10 mutations that can be easily made as stated by the Applicants. The invention requires one skilled in the art to locate a region with 1-10 nucleotides in the DNA sequence of 4804 nucleotides of SEQ ID NO: 2, then generate an unspecified number of mutants by conservative and/or non-conservative amino acid substitution, or deletion or insertion or addition or in combination (using a genetic code Table), then characterize those mutants to determine if they have the property to interact with cAMP-GEFII, However, the specification does not give the description. Therefore, one skilled in the art would have to find

for themselves that what the claimed mutant does, and this falls short of meeting the requirements of full scope of enablement. For the reasons set forth above, undue experimentation is necessary to make and use the claimed mutants encoding a protein that retains the property of interacting with cAMP-GEFII.

Claim 8 is directed to a fragment of a DNA sequence set forth in SEQ ID NO: 2. The specification fails to provide any description of the structure and function of the fragment claimed. While the specification at page 5 defines the fragment as a DNA fragment consisting of a part of any one of the DNAs set forth in full length sequence set forth in SEQ ID NO: 2 or in the mutant sequence thereof, however, there is no disclosure about the biological activities of the claimed fragments. Without any guidance or suggestions a skilled artisan would not be able to predict the structure of a fragment that would demonstrate the same activity as the activity of the full length DNA sequence of SEQ ID NO: 2. In response Applicants urge (Response page 6, paragraph 3) that one of ordinary skill in the art make DNA fragments of known and unknown sequences as part of their everyday activities. Further, identification of a sequence as a fragment of SEQ ID NO: 2 is easily accomplished through use of a multitude of DNA analysis software. Applicants' arguments not fully address the rejection. The issue is not how to generate DNA fragments randomly from a given DNA sequence, the issue is as stated above the biological activities of the claimed fragments. There is no disclosure about the biological activities of the claimed fragments. Thus, for the reasons set forth above, undue experimentation is required to make and use the claimed fragments.

Claim 10 is directed to a primer consisting of a partial sequence of the DNA sequence set forth in SEQ ID NO; 2. Specification fails to provide the specific sequence of the primer that would anneal to the DNA template of a sequence set forth in SEQ ID NO: 2. Applicants' urge (page 7, paragraph 2) that creation of a primer is such a basic step in molecular biology, i.e. for sequencing, PCR, or replication (?), that one of ordinary skill in the art could easily create a primer, if given a DNA sequence. However, as stated above the specification fails to provide the specific sequence of the primer that would anneal to the DNA template of a sequence, which is 4980 nucleotides long set forth in SEQ ID NO: 2. Therefore, one skilled in the art would have to

find for themselves that what the claimed primers structures are that would anneal efficiently to a template selected from an undefined region of a sequence of SEQ ID NO: 2 which has 4980 nucleotides. Therefore it requires undue experimentation to design and develop a suitable primer for practicing the invention given the current claim.

3) The predictability or unpredictability of the art;

The invention is highly unpredictable for the reasons set forth for factors 1 and 2 above.

4) The amount of direction or guidance presented;

5) The presence or absence of working examples; and,

6) The quantity of experimentation necessary:

The claims are directed to a mouse DNA that encodes the protein of SEQ ID NO: 1 and a mutant thereof; and a DNA sequence set forth in SEQ ID NO: 2 corresponds to protein of SEQ ID NO: 1 and fragments thereof. However, the specification provides only a generic description of how a variety of mutants can be generated (page 7), no specific guidance is provided on the generation of the mutants or fragments that demonstrate the biological activity of the full length protein or DNA sequences. There are no working examples of these variants in the specification. While the specification in Example (page 14, lines 15-22, Fig. 4), and at page 9, lines 4-16 describes and demonstrates that the full length DNA set forth in SEQ ID NO: 2 encoding the protein of SEQ ID NO: 1 is asserted to interact with cAMP-GEFII, there is no disclosure about the biological activities of the claimed mutants. Since the specification fails to provide sufficient guidance on the structure and function of the various mutants and fragments, it is necessary to have additional guidance on the identities of mutants/fragments to carry out further experimentation to assess their property of interacting with cAMP-GEFII.

7) The state of the prior art; and,

8) The relative skill of those skilled in the art:

The prior art has shown a cDNA with 5640 bp from a rat brain library, which encodes a large protein RIM2 with 1555 amino acid residues, RIM2 cDNA has 75.8% sequence identity to SEQ ID NO: 2 (see Wang's reference cited in previous office action), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the structure and function for various protein/ DNA products to be considered enabling for variants.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because in summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the guidance/the teaching in the specification is limited, and the outcome is unpredictable for the various modified forms, it is necessary to have additional guidance and to carry out further experimentation to assess the property of the variants. Therefore, due to large quantity of experimentation necessary to determine an activity or property of the disclosed gene and the modified forms thereof, such that it can be determined how to use the claimed gene, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the specification fails to teach the skilled artisan how to make and use the claimed invention.

Rejections under 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 5, 8 and 10 remain/are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite because of the phrase with one to ten nucleotides deleted, substituted, inserted, or added relative to the nucleotide sequence set forth in SEQ ID NO: 2, which has 4980 nucleotides. Furthermore, the position of these nucleotides in relation to the sequence of SEQ ID NO: 2 is also not clear, nor is whether or not the claim is intended to have

only 1 to 10 or would have included at least 1-10 nucleotides inserted, substituted, deleted in one or multiple combinations thereof.

Claim 8 is indefinite as to what part is the part that claim 8 refers to that is from claim 4. The amendment to the independent claim 4 does not correct the deficiency of the dependent claim 8.

Claim 10 is indefinite because of the term "partial sequence." The term "partial sequence" renders the claim indefinite. It is not clear how many nucleotides are there in this partial sequence that the primers consist of. Also what is the position of the primer sequence relative to the sequence of SEQ ID NO: 2 of claim 4? Applicants urge at page 9, last paragraph that "partial sequence' means a DNA sequence which has 100% homology with SEQ ID NO: 2, or a mutated SEQ ID NO: 2 as claimed in claim 5, but is not "full length." However, Applicants response does not fully address the rejection as indicated above.

New ground of rejection

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (Nature vol. 388, pp 593-598, August 1997, IDS Reference No. 1). Wang et al. teach a RIM protein encoded by a cDNA isolated from a rat brain library, which encodes a large protein RIM with 1553 amino acid residues (see page 593, col. 2, and Fig. 1, page 594). This reads on claim 3 which is a purified mouse DNA that encodes a protein having amino acid sequence of SEQ ID NO: 1, and also on claim 5 which has any number of insertions, deletions and/or substitutions both singly and/or in any combination. Claim 4 is also rejected because absent factual evidence to the contrary, the reference discloses a DNA that corresponds to DNA encoding the protein. Since claim 6 only requires a claim 4 DNA corresponding to a protein of claim 3 (i.e. does not require 100% amino acid sequence identity) thus, absent factual data to the contrary it would

have been anticipated that the reference disclosed DNA encoding a protein corresponding to the protein of claim 3. As to claim 8, the Wang et al. reference discloses variants (see page 593, col 2) that are/would have been those fragments that consist of part of the DNA of claim 4. Thus claims 3-8 of the instant application are anticipated by Wang et al.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al. (WO 98/31802, July 23, 1998). Jacobs et al. teach a cDNA that hybridizes with SEQ ID NO: 2 of claim 9 (see alignment result, Database: N_Geneseq_0601, AC NO: AAV40485). Therefore, Jacob's DNA is considered for a probe as claimed in claim 9 of the instant application.

As to primers, the claim 10 primer is to hybridize to the DNA of claim 4, which any DNA corresponding to the protein of claim 3. The Jacobs et al. reference discloses such DNA encoding a protein corresponding to the protein of claim 3, thus it is anticipated that the strand complementary to the coding strand would have been a primer.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the

status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.

October 18, 2002

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